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Dockets Management Branch (HFA-305)
Room 1061
Food and Drug Administration
5630 Fishers Lane
Rockville, MD
20852

REF: Docket No. 99N-4166

Attached are Baxter Healthcare Corporation's comments regarding the collection of information for 2 1 CFR Part 11, Electronic Records; Electronic Signature.

If we may provide further information, please contact the undersigned.

Sincerely,

Richard Farb

Richard Farb
Corporate Director, Regulatory Affairs

99N-4166

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SUMMARY:

The Paper Work Reduction Act of 1995 (PRA)' requires Federal agencies to obtain approval from the Office of Management and Budget (OMB) for each collection of information they sponsor. The FDA requested public comment (RPC) regarding extension[2] of collection of information required by 21 CFR Part 11 Electronic Records; Electronic Signatures (Part 11). The FDA invited comment on: (1) Whether the proposed collection of information is necessary for the proper performance of the FDA's functions, including whether the information will have practical utility; (2) The accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) Ways to enhance the quality, utility, and clarity of the information to be collected; and (4) Ways to minimize the burden of the collection of information on respondents, including the use of automated collection techniques, when appropriate, and other forms of information technology.

Baxter Healthcare Corporation (Baxter) would like to comment on each of these issues.

GENERAL:

Baxter has reviewed recent interpretations of compliance requirements with Part 11 and finds that the FDA's estimates and assumptions are not consistent with Baxter's experience. The estimated cost to Baxter is actually several orders of magnitude greater than the FDA's estimate.

RESPONSE:

(1) Whether the proposed collection of information is necessary for the proper performance of the FDA's functions, including whether the information will have practical utility.

Part 11 has significantly extended the requisite data collection and management well beyond those in prior versions of 21 CFR. This extension includes the redefinition of "original data" and expansion of the types of computer systems covered by the regulation. The redefinition of "original data" includes signals from laboratory and process control equipment. Current industry practice involves maintaining paper printouts and charts generated by this equipment as official documents. The electronic signals now must be archived to meet regulatory data retention requirements. This creates a major new burden of data collection and maintenance without improving the quality of the information.

Part 11 also includes restrictive data archival and management requirements. Section 11.10 (b) limits industry's ability to employ advances in technology by requiring that industry be able to create electronic copies of their records and that they check with the

[1] Ref: 44 U.S.C. 3501-3520
[2] OMB Control Number 0910-0303

agency if there is any question regarding the agency's ability to review and copy these records.

Sections 11.10 (e), 11.10 (k) and 11.10 (a) (2) require recording of the time that events occur. Although date-time stamping is typically a standard function of computer programs, the FDA has added an additional requirement for documentation of the local time zone[3], which is not a normal feature of computer programs. The requirement to document time has created additional manual record collection burden. When both manual and computer systems are used for data collection, time will be required on the paper document as well as in electronic records in order to verify time sequenced events, as required in Section 11.10 (f).

Unlike current record archival requirements that allow data to be stored in a number of formats including paper, microfilm and microfiche, electronic records must be stored only in electronic format. This has created an additional burden for industry in that the retention period for most records is beyond the normal life expectancy of storage media. This is also beyond current requirements for governmental record storage as determined in General Records Schedule 20 (GRS 20); Disposition of Electronic Records[4]. GRS 20 requires each federal agency to dispose of word processing and electronic mail files once they have been copied to a paper or electronic record keeping system.

(2) The accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used.

Baxter's examination of assertions included in the RPC finds that assumptions used to develop estimates of the impact of Part 11 on regulated industry were not based on real life experience. Baxter's comments regarding each RPC statement follows. The RPC statements are presented in ***italics*** followed by description of the issues associated with each statement.

"The burden created by the information collection provision of this regulation is a one-time burden associated with the creation of standard operating procedures, validation and certification."

The information collection provision of this regulation is an ongoing rather than one time burden. The ongoing burden is a result of the FDA's gradual release of guidance documents related to Part 11. These guidance documents further define the expectations of the Agency and, as such, require industry to modify procedures and systems to reflect these new expectations.

In listing only creation of standard operating procedures (SOPs), validation and certification as burdens created by Part 11, the FDA fails to recognize the burden created

[3] Computerized Systems Used in Clinical Trials, Section V.C.
[4] 60 Fed. Reg. 44,643 (1995)

by the unusual decision to not grandfather existing systems. By not excluding legacy systems, the FDA has added modification of programs and system documentation to the burden. This effort is significantly greater than that required to develop standard operating procedures.

Validations are performed in two main circumstances; (1) implementation of new processes and (2) modification of existing processes. By including validation in the list of burdens created by Part 11, the FDA recognizes modification of existing systems as a burden produced by the failure to grandfather existing system.

"The record keeping provisions in Part 11 (§§ 11.10, 11.30, 11.50, 11.300) require standard operating procedures to assure appropriate use of, and precautions for, systems using electronic records and signatures"

Part 11 calls for the employment of procedures and controls, not SOPs. By including only the burden of creating SOPs, the FDA has failed to evaluate the procedures and controls of Part 11 that can only be met through the use of software. Examples of Section 11.10 requirements that necessitate software-based procedures include (underlines added for emphasis):

> "(b) The ability to generate accurate and complete conies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency. Persons should contact the agency if there are any questions regarding the ability of the agency to perform such review and copying of the electronic records."
> "(c) Protection of records to enable their accurate and ready retrieval throughout the records retention period."
> "(e) Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records."
> "(f) Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate."
> "(g) Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand."
> "(h) Use of device (e.g., terminal) checks to determine, as appropriate, the validity of the source of data input or operational instruction.

In addition to merely creating a burden of generating of SOPs, the above requirements create a burden of modification of computer systems and their associated documentation that were designed and implemented before Part 11 became effective. The failure to grandfather existing systems places the industry in the position of focusing time and dollars on remediation, rather than implementation of new and better computer systems.

The requirement to provide the FDA with copies of software, as well as data, creates a legal burden for the industry. Most major systems employ proprietary software packages that include licensing requirements regarding number of users and installations. The

requirement that industry provide copies places industry in the position of violating or renegotiating licensure agreements in order to comply with Part **11.**

The Archivist of the United States promulgated GRS 20 to authorize the archival of electronic records to either paper or electronic record keeping systems. In disallowing this practice, Sections 11.10 (c) and 11.10 (e) create an ongoing burden for industry that is not in agreement with the US Government's own policy regarding archival of data. Failure to authorize archival of electronic records to paper or some other more permanent storage media, forces the industry to develop and maintain procedures for conversion of data to new storage formats. Each conversion must be validated to ensure that original data plus audit trail and metadata are successfully transferred during each conversion. Even after the conversion of one system to another, the FDA expects that industry maintain all software for the old system. They also expect industry to have a strategy for reconstructing the system during an investigation, either by retaining hardware or through contracts with a vendor to retain the hardware. This is unnecessary if there has been a complete, successful and validated migration of data.

The requirement for date-time stamping all records is restrictive. Use of date-time stamps does not meet the requirement of 11.10 (f) for enforcing the timed sequence of events as well as internal validated program constructs that force entries to occur in a specific order. In addition, it is much harder to by-pass a hard-coded requirement than changing the time clock of a particular workstation or system. Date-time stamping creates the ongoing burden of coordinating the internal clocks of multiple systems.

The FDA recognizes that Part 11 creates a burden on industry related to bringing legacy systems into compliance. This is evidenced in Compliance Policy Guide 7153.1 1- Enforcement Policy: 21 CFR Part 11; Electronic Records; Electronic Signature (CPG 7153.11) issued 1999. The background section of CPG 7153.11 contains the following statement:

> "Certain older systems may not have been in full compliance with Part 11 by August 20, 1997, and modifications to these so called "legacy systems" may take more time. As explained in the Preamble to the final rule, Part 11 does not grandfather legacy systems and the FDA expects that firms using legacy systems will begin taking steps to achieve full compliance. "

The policy defined by CPG 7153.11 indicates that decisions on whether or not to pursue regulatory action will be based on a case by case evaluation using the following criteria:

- Nature and extent of Part 11 deviation(s)
- Effect on product quality and data integrity
- Adequacy and timeliness of planned corrective measures
- Compliance history of the establishment, especially with respect to data integrity

The guidance document's authorization for handling compliance on a case by case basis could create a situation where Part 11 is enforced differently by the various FDA regional offices. Further, industry resources have been focused on Year 2000 priorities since before August 1997, Legacy system modification planning may not have progressed due to conflicting priorities.

"The reporting provision (§ 11.100) requires that persons certify in writing to FDA that they will regard electronic signatures used in their systems as the legally binding equivalent of traditional handwritten signatures."

The FDA's estimate of the burden caused by Section 11.100 does not take into account multi-national corporations. It is unreasonable to expect corporations, which are made up of diverse business units, to submit a single certification to the agency. Each of the corporation's business units must evaluate its position regarding electronic records and signatures and submit a certification for the business unit.

The estimate of the burden caused by Section 11.100 fails to include the following requirement of Section 11.100 (c) (2):

> "Persons using electronic signatures shall, upon agency request, provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature."

This section adds the additional burden of collection and storage of a certification from each computer system user that they accept electronic signature as equivalent to their handwritten signature. These certifications must be kept on file and current in case of an agency request.

In Table 1, the FDA estimates the annual reporting burden for Section 11.100 to one (1) hour/respondent, The estimate assumes that each corporation will make one submittal. In actuality, Baxter's business units will make a minimum of five (5) submissions.

Table 1 does not include an estimate for the additional burden created by Section1 1.100 (c) (2) that persons using electronic signature provide upon agency request additional certification that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature. This requirement creates an ongoing burden of maintaining certification for all persons signing electronic records. This effort involves a total of 30 minutes per user per system, in the following time increments:

Form Initiation - 5 minutes
User training - 15 minutes
Document Review - 5 minutes
Document Filing - 5 minutes

A typical Baxter employee uses 3 - 5 computer systems, each of which has a unique electronic signature, as part of their normal activities. This means that the actual time required per employee is 90 - 150 minutes. The initial burden created by Section1 1.100 (c) (2) is 30,000 to 50,000 hours. In addition to the initial burden, implementation of new systems will create an annual burden of 5,000 to 10,000 hours.

"There are no capital costs or operating and maintenance costs associated with this collection of information. "

Bringing legacy systems into compliance with Part 11 creates added capital costs for industry since many existing systems were developed using hardware and software platforms that cannot meet the requirements of Part 11. This will require either upgrading legacy systems to versions that can be made compliant or total replacement of those systems. The capital costs are substantially increased when systems must be replaced before the end of their expected life in order to comply with Part 11.

In some cases, technology needed to bring systems into compliance is not currently available. This is particularly true with laboratory equipment for which new technology must be developed, at great cost, to achieve rudimentory compliance with Part 11.

The above assumption that there are no maintenance costs is flawed. It ignores the Part 11 requirement to maintain records in electronic format for the full retention period. The maintenance costs for archival of electronic records is significantly higher than the cost for archiving records in other formats. Added costs include refresh of media, conversion of records to new formats to keep up with technology and validation of the both the new storage technology and record conversion.

In preparing the estimate of cost, the FDA failed to consider the cascading impact of Part 11. For example, Table 2 assumes that development of a single set of SOPs is adequate to bring a corporation into compliance with the rule. In the case of multi-national corporations, such as Baxter, whose business units are covered by multiple, diverse regulations, a tiered approach to operations management is required. This approach includes: (1) a corporate policy statement, (2) business unit operating procedures, (3) facility specific operating procedures, and (4) system operations manuals. Therefore, in Baxter's case, the number of SOPs required is more than fifty times the estimate in Table 2. Table 2 also fails to consider Systems Operations Manuals that are required to define system specific compliance procedures. Baxter's actual experience is as follows:

1. Creation of Baxter's corporate policy involved a team of 10 people who worked for 2 days to develop an outline of the document. A sub-team of 5 people worked for a month finalizing and activating the document. A total of 880 hours were required to implement the corporate policy.

2. Development of a business unit's SOP typically involves a minimum of three (3) individuals approximately one week or a total of 120 hours to develop and activate. Baxter's five business units have committed more than 600 hours to this effort.

3. Operating procedures defining requirements for each manufacturing plant and technical support center must be developed following creation of the Business Unit SOP. Development of these documents typically requires the same development and activation time as required for business unit operating procedures. Baxter's fifty manufacturing plants and technical support centers have committed more than 6000 hours to implementation of these procedures.

4. Modification of system operations manuals to address electronic records and electronic signatures typically requires 5 to 10 hours per system. An average manufacturing facility or technical support center has 10 computer systems that are impacted by Part 11, meaning that a total of 50 - 100 hours are required per operation to bring this documentation into compliance. Baxter's total record keeping burden for this activity is 2500 - 5000 hours.

Baxter's overall estimate of time reasonably required for the creation of of SOPs is 9,980 to 12,480 hours, which is significantly higher than the 80 hour estimate found in Table 2.

(3) Ways to enhance the quality, utility, and clarity of the information to be collected

The quality and utility of information to be collected could be improved significantly by providing a clear definition of the difference between electronic data and electronic documents. Predicate rules, such as 21 CFR 211 and 820, provide clear definition of the difference between Master Records and Batch Records. Master Records, which are intended to assure uniformity from batch to batch, are typically in document format, Batch Records, which are intended to document the actual production process, are typically made up of finite elements or data. Part 11 should provide for the same distinction between these records.

As Master and Batch Records are managed differently, Part 11 should also provide for an audit trail process that meets the needs for assuring the accuracy of each record. In the case of Master Records, this should involve typical document management procedures including initial draft development, review and comment and final document issuance. Official electronic audit trail should only involve tracking of official final document versions.

Audit trail for Batch Records, which represent information that cannot be reproduced, must provide a higher level of assurance. This audit trail should begin with the initial creation of a record and end only when the regulatory retention period has expired.

(4) Ways to minimize the burden of the collection of information on respondents, including the use of automated collection techniques, when appropriate, and other forms of information technology

Two changes made to the requirements of Part 11 would mitigate the burden of collection of information. First, legacy systems should be grandfathered to make Part 11 consistent with normal FDA regulations, If grandfathering is not acceptable, then a moratorium on issuance of 483 items and warning letters should be put in place for a period of at least 3 years. This period is necessary because of the lack of technology to meet some Part 11 requirements.

Second, authorization to archive electronic records to paper or other permanent media should be added to the rule. If the archival were authorized at the end of the expected life of the original storage media, it would provide the FDA with the opportunity to audit current information using automated systems. It would also eliminate the considerable cost burden of maintaining obsolete hardware and software of decommissioned systems.